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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,287	05/10/2001	Robert Klein	R00208US (#9	1252

7590 08/11/2003

D Peter Hochberg Company
6th Floor
1940 East 6th Street
Cleveland, OH 44114-2294

EXAMINER
GHALI, ISIS A D

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/11/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,287	KLEIN ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9 and 11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' request under 1.114 and preliminary amendment C, both filed 5/30/2003.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/30/2003 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3-9 and 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,954,343 ('343) in view of any of US 5,683,711 ('711) or WO 97/23227 ('227).

Claim 1 reads as a transdermal therapeutic system comprising backing layer, a protective release liner, and a reservoir comprising polyacrylate adhesive, amino group containing polymer and combination of estradiol and norethisterone. The amino-group containingg polymer is selected from polyaminoamides, polyaminoimidazolines, polyurethaneamines, polyamines and polyglucosamines.

US '343 teaches a dermal pharmaceutical preparation comprising a pressure sensitive adhesive comprising acrylic adhesives and a drug to be delivered by this preparation such as progesterone and estradiol, used individually or in combination in an amount of 0.1 to 30 % (col.2, lines 41-43; col.4, lines 21-31, 45-47, 56-59; col.5, lines 31-32). The acrylic adhesive, inherently, consists of carbon, hydrogen and oxygen. The dermal preparation further comprising copolymer having an amino group to maintain the drug in a dissolved state at high concentration without undergoing crystallization and

further exhibits excellent adhesion to the skin (abstract; col.1, lines 30-45; col.4, lines 56-58). The adhesive layer (reservoir) has a thickness of 5 to 1000 micrometer and has a support layer (col.4, lines 60-67).

Although US '343 recognized the prevention of crystallization of high concentration of drugs by including amino group containing polymers in the adhesive composition, the reference does not teach the presence of estradiol and norethisterone in supersaturated state in the reservoir or the particular amino group-containing polymers.

It is within the skill in the art to select species when the genus is disclosed. The instantly claimed amino group-containing polymers do not impart patentability to the claims, absent evidence to the contrary.

US '711 teaches a transdermal patch comprising estradiol and norethisterone in a supersaturated state in acryl ate adhesive matrix and the viscosity of the adhesive matrix can inhibit crystallization of the supersaturated adhesive (col.6, lines 31-35, 61-62; col.8, lines 41-47; col.9, lines 23-25; col.10, lines 52-58). The reference teaches that the supersaturation is desirable and necessary in order to impart a high thermodynamic activity to drugs which permeate with difficulty (col.6, lines 40-45). The amount of estradiol/NETA is 2.5%/10% (col.10, Table 3).

WO '227 teaches a transdermal patch for release of estradiol and progesterone comprises a backing layer; a protective release liner; and an active ingredient pressure sensitive adhesive matrix layer containing combination of estradiol and norethisterone acetate and crystallization inhibitor (abstract; page 4, first and forth paragraphs; page 7,

first full paragraph). The pressure sensitive adhesive matrix layer is acrylate copolymers (page 5, last paragraph). The matrix includes estradiol and norethisterone (NETA) in a supersarurated state. The estradiol is between 0.6 to 1.8 % and the NETA is between 4.0 to 10.0 % (page 6, last paragraph). The pressure sensitive adhesive is solvent based (Example 1, page 8). The reference teaches that the transdermal patch comprising estradiol and NETA in supersaturated state in the copolymeric matrix is the condition which confers to the active ingredients activity required for a forced diffusion through the skin even in absence of absorption enhancer, and could release constant amounts of the drugs during its whole possible application time from 3-7 days (page 4, last paragraph; page 6, last paragraph).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device comprising a reservoir of acrylate adhesive comprising high concentration of estradiol and NETA and amino group containing polymer as disclosed by US '343, and replace the high concentration of the hormones by supersaturated state of the hormones as disclosed by any of US 711 and WO '227, motivated by the teaching of US '711 that the supersaturation is desirable and necessary in order to impart a high thermodynamic activity to drugs which permeate with difficulty, or motivated by the teachings of WO '227 that the transdermal patch comprising estradiol and NETA in supersaturated state in the copolymeric matrix is the condition which confers to the active ingredients activity required for a forced diffusion through the skin even in absence of absorption enhancer, and could release constant amounts of the drugs during its whole possible application

time from 3-7 days, with reasonable expectation of having a transdermal delivery device comprising a combination of estradiol and NETA in a supersaturated state without crystallization with great success.

Response to Arguments

5. Applicant's arguments with respect to claims 1, 3-9 and 11-18 have been considered but are moot in view of the new ground(s) of rejection.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Isis Ghali
Examiner
Art Unit 1615

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600